REMARKS

Claims 32-93 presently appear in this case. No claims have been allowed. The official action of August 21, 2003, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to a reactive probe chip for detecting target functional molecules. A first carrier probe, in the form of porous particles, is prepared having a first reactive substance capable of bonding a first target molecule immobilized within the pores thereof. A second carrier probe, in the form of a porous particle, is also prepared having immobilized within the pores thereof a second reactive substance capable of bonding a second target molecule. The first and second carrier probes are immobilized on a surface of a substrate material in order to form the reactive probe chip. This probe chip is preferably a DNA chip having a plurality of different carrier probes, each disposed in a discrete microcompartment of the substrate.

The interview among Examiner Siew, the undersigned attorney, one of the inventors, Dr. Nagasawa, and a representative of assignee, Ms. Maki Yamaji, conducted on January 29, 2004, is hereby gratefully acknowledged. In this interview, proposed new claims were discussed, as was additional prior art, which will be supplied in an Information Disclosure Statement. The arguments presented as the substance of the interview will be repeated in the discussion of the prior art hereinbelow. The claims as discussed at the

interview have been further amended somewhat and are presented herewith.

The examiner has reconsidered the restriction requirement and rejoined Groups I and II. Accordingly, all the claims now present in the case are currently being examined.

Claims 29-31 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The examiner states that claims 29-31 lack active steps and that claim 28 is unclear as it cannot be determined to what process would be like polishing.

Claims 28-31 have now been deleted without prejudice. The indefinite terminology no longer appears in the newly presented claims. Accordingly, this rejection has now been obviated.

Claims 1-25 and 27-31 have been rejected under 35 U.S.C. §102(b) as being anticipated by Bauman. The examiner states that Bauman teaches a composite substrate with a plurality of porous regions arrayed on and comparted by non-porous regions. The examiner states that the porous material is derived from various substrates whose total surface is a porous solid, and the surface is processed by cold pressing or slip casting. The examiner states that antibodies that have specific binding to epitopes are used and that porous glass is disclosed with a pore size of 5-100 microns. The examiner states that the product can be fabricated by immobilizing a probe on a particular carrier and arraying and immobilizing

each of the loaded carriers in a separate compartment in the base materials in wells with widths of around 8-12 mm and depths of 4-6 mm. This rejection is respectfully traversed.

All of the previously-appearing claims have now been deleted. New claim 32 requires carrier probes in the form of a porous particle having a first reactive substance immobilized within the pores thereof. A second porous particle carrier probe is also present having a second target molecule immobilized within the pores thereof. The first and second carrier probes are then immobilized on a surface of a substrate material. In the course of the interview, the Bauman disclosure was discussed. At column 4, lines 40-42, Bauman states that the analyte/indicator complex may be colored ceramic particles with the analyte/indicator complex coupled thereto. However, at no time in Bauman are the colored particles immobilized on the substrate, as is required by all of the present claims. It is critical that the colored particles be able to move freely through the pores so as to allow a visible representation of the amount of analyte in a sample. Thus, in Bauman, if more than one carrier probe were used, there is a possibility of the particles mixing together. Once these particles are mixed, the reactive probe chip cannot be used as a reactive probe chip.

Furthermore, there is no indication in Bauman that the colored particles are themselves porous. The present claims specify that the carrier particles are porous and that the reactive substances are immobilized within the pores of

the carrier particles. In Bauman, the probes are only immobilized on the outer surface of the beads. If beads having probes on the outer surface are stored in a bottle, the beads will contact one another and the probes on the outer surface may be damaged. In the present invention, the probes are immobilized within the pores. Thus, even if the particle carriers of the present invention contact one another while stored in a bottle, the probes within the pores will not be damaged. Furthermore, when the reactive substance is immobilized within the pores, the probes will be more stable during reaction with the target molecules than those on the surface of the beads because the flow velocity of the sample in the pores is lower than that at the outer surface of the beads.

At the interview, the examiner stated that he was interpreting the porous ceramic as being itself a carrier probe with the sheath being the substrate. He pointed out that claim 32 did not specify the size of the particle. However, the term "particle" has a meaning and cannot encompass the entire substrate 12 of Figure 1 or substrate 104 of Figure 15. There is no way that these substrates can be considered to be a one or more particles. Furthermore, even if this carrier is interpreted as being a porous particle carrier, the probes are not immobilized thereon.

Additionally, claim 32 requires a first and a second carrier probe, both of which are immobilized on the surface of a substrate material. If the sheath is considered to be a

substrate material in the broadest sense, there is still no disclosure of having more than one different carrier probe placed on any kind of substrate material. There is always only a single reactive substance throughout the porous ceramic material. If two reactive substrates were to be used, the first and second reactive substances may be mixed together making it impossible to detect targets. Accordingly, none of the present new claims are anticipated by Bauman. Reconsideration and withdrawal of this rejection are respectfully urged.

Claim 26 has been rejected under 35 U.S.C. §102(b) as being anticipated by Wickstrom. The examiner states that Wickstrom teaches a method of producing an oligonucleotide on a solid phase support, such as glass porous particles.

Claim 26 has now been deleted and no claims of the scope of claim 26 presently appear in the case. None of the claims presently appearing in the case are anticipated by Wickstrom. Accordingly, reconsideration and withdrawal of this rejection are respectfully urged.

Attached hereto is an Information Disclosure Statement, making of record certain additional references that the examiner may consider to be pertinent. Two of these, Southern and Kambara, were discussed at the interview and distinguished from the present claims. The third was noted by the examiner in the course of the interview and was also discussed at the interview. The arguments presented at the interview will be presented herein.

Southern discloses a method for synthesizing oligonucleotides on a solid phase substrate, such as controlled pore glass or a plain glass surface. Example 3 discloses preparing derivatized glass beads and then causing them to be adhered to a stick.

Southern does not consider the substrate to be critical. Note column 2, lines 17-18, which explicitly states that the nature of the support is not critical to the invention. Although porous glass particles are disclosed, there is no suggestion that such particles would have any advantages over any other smooth substrate, such as a plain glass bead, which is also disclosed. Furthermore, the stick of Example 3 is substantially different from a DNA chip, which uses a very small amount of such particles and the amount of oligonucleotide that can be packed on a given particle becomes very important in order to establish the necessary sensitivity. Southern does not disclose the use of plural kinds of porous particle carrier probes disposed on a substrate. With the present invention, a plurality of carrier particle probes can be prepared beforehand and then only those needed for a given application may be selected and applied to the DNA chip. Thus, only the specified target molecules may be detected without detecting unnecessary molecules that may relate to sensitive personal data. None of this is suggested by Southern.

Kambara is directed to a DNA probe array that uses small particles which are spherical, such as beads (see column

2, lines 55-56). These are not porous beads. In Kambara, the DNA probes are first prepared by synthesis and thereafter they are modified to add a functional group to facilitate binding to a surface, and then they are fixed on the surfaces of the beads. The advantages of porous glass beads over spherical beads has already been discussed above with respect to Bauman. Furthermore, growing the probes on the beads, as is required by some of the present claims, is substantially advantageous as the probes can be damaged if they are first synthesized, functionalized and then disposed on the beads by means such as avidin and biotin. Accordingly, none of the present claims are anticipated or made obvious by either Southern or Kambara.

The examiner mentioned the Uo patent at the interview for its disclosure in column 2, lines 32-33, that porous bead carriers are used in ELISA assays. However, the examiner, at the interview, conceded that in ELISA assays the beads are not immobilized on a substrate. As all of the present claims require that the beads be immobilized on a substrate, they are not anticipated by Uo. Furthermore, a plurality of carrier particle probes are immobilized on the substrate in the present invention while Uo discloses only one kind of carrier particle probes. Accordingly, Uo does not anticipate or make obvious any of the present claims.

For all of these reasons, it is submitted that all of the claims now present in the case fully comply with 35 U.S.C. §112 and clearly define over the references of record.

Reconsideration and allowance are, therefore, earnestly solicited.

Respectfully submitted,

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